

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing of claims in the application.

1. (Original) An antibody comprising an Fc variant portion comprising at least one amino acid modification in the Fc region of said parent Fc polypeptide, wherein said Fc variant modulates binding to an FcγR as compared to the parent Fc polypeptide.
2. (Original) An antibody according to claim 1 wherein said modulation is an increase in affinity of said antibody to said FcγR.
3. (Original) An antibody according to claim 1 wherein said Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 234, 235, 239, 240, 241, 243, 244, 245, 247, 262, 263, 264, 265, 266, 267, 269, 296, 297, 298, 299, 313, 325, 326, 327, 328, 329, 330, 332, 333, and 334.
4. (Original) An antibody according to claim 1, wherein said Fc variant comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 240, 244, 245, 247, 262, 263, 266, 299, 313, 325, 328, and 332.
5. (Original) An antibody according to claim 1, wherein said Fc variant comprises a substitution at position 332.
6. (Original) An antibody according to claim 1, wherein at least one substitution is at a position selected from the group consisting of: 239, 264, 297, and 330, with the proviso that if said sequence is substantially human, said substitution is not S239A, V264A, N297A, N297Q, A330D, A330Q, A330K, or A330S.
7. (Original) An antibody according to claim 1, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234E, 234N, 234Q, 234T, 234H, 234Y, 234I, 234V, 234F, 235D, 235S, 235N, 235Q, 235T, 235H, 235Y, 235I, 235V, 235F, 239D, 239E, 239N, 239Q, 239F, 239T, 239H, 239Y, 240I, 240A, 240T, 240M, 241W, 241L, 241Y, 241E, 241R, 243W, 243L, 243Y, 243R, 243Q, 244H, 245A,

247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L, 264I, 264W, 264T, 264R, 264F, 264M, 264Y, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H, 265T, 266I, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325T, 325V, 325H, 327N, 327L, 328M, 328D, 328E, 328N, 328Q, 328F, 328I, 328V, 328T, 328H, 328A, 329F, 330L, 330Y, 330V, 330I, 330F, 330R, 330H, 332D, 332E, 332N, 332Q, 332T, 332H, 332Y, and 332A.

8. (Original) An antibody according to claim 1, wherein said Fc variant is selected from the group consisting of 264L, 264I, 241W, 241L, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, 241L/262I, 243L/264I, 243L/262I/264W, 241Y/243Y/262T/264T, 241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, 332E, 328M/332E, 244H, 245A, 247V, 313F, 244H/245A/247V, 247G, 264I/332E, 241E/243R/262E/264R/332E, 241E/243Q/262T/264E/332E, 241R/243Q/262T/264R/332E, 241E/243Y/262T/264R/332E, 298A/332E, 239EI/332E, 239Q/332E, 239E, 265G, 265N, 239E/265G, 239E/265N, 239E/265Q, 296E, 296Q, 299I, 327N, 267Q/327S, 267L/327S, 327L, 329F, 330L, 330Y, 332D, 297S, 297D, 297S/332E, 297D/332E, 297E/332E, 265Y/297D/332E, 265Y/297D/299L/332E, 265F/297E/332E, 328I/332E, 328Q/332E, 332N, 332Q, 264T, 264F, 240I, 263I, 266I, 299A, 299S, 299V, 325Q, 325L, 325I, 239D, 239N, 239F, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239N/332N, 239NI/332Q, 239Q/332D, 239Q/332N, 239Q/332Q, 296D, 296N, 241Y/243Y/262T/264T/297D/332E, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234D, 234E, 234N, 234Q, 234T, 234H, 234Y, 234I, 234V, 234F, 235D, 235S, 235N, 235Q, 235T, 235H, 235Y, 235I, 235V, 235F, 239T, 239H, 239Y, 240A, 240T, 240M, 263A, 263T, 263M, 264M, 264Y, 266A, 266T, 266M, 269H, 269Y, 269F, 269R, 296S, 296T, 296L, 296I, 298H, 299H, 330V, 330I, 330F, 330R, 330H, 325D, 325E, 325A, 325T, 325V, 325H, 328D/332E, 328E/332E, 328N/332E, 328Q/332E, 328V/332E, 328T/332E, 328H/332E, 328I/332E, 328A, 332T, 332H, 332Y,

332A, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239E/264I/298A/330Y/332E, 239D/297D/332E, 239E/297D/332E, 239D/265V/297D/332E, 239D/265I/297D/332E, 239D/265L/297D/332E, 239D/265F/297D/332E, 239D/265Y/297D/332E, 239D/265H/297D/332E, 239D/265T/297D/332E, 264E/297D/332E, 296D/297D/332E, 296E/297D/332E, 296N/297D/332E, 296Q/297D/332E, 296H/297D/332E, 296T/297D/332E, 297D/299V/332E, 297D/299I/332E, 297D/299L/332E, 297D/299F/332E, 297D/299H/332E, 297D/299E/332E, 297D/330Y/332E, 297D/298A/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.

9. (Original) An antibody according to claim 7, wherein said Fc variant portion further comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.
10. (Original) An antibody according to claim 1, wherein said Fc γ R is Fc γ RIIIa.
11. (Original) An antibody according to claim 10, wherein said Fc γ RIIIa is a V158 or F158 allotype of Fc γ RIIIa.
12. (Original) An Fc variant according to claim 2, wherein said parent Fc polypeptide is substantially human, and said affinity is approximately 5-fold greater than that of said parent Fc polypeptide.
13. (Original) An antibody according to claim 12, wherein said parent Fc polypeptide is substantially human, and said affinity is between about 5-fold and about 300-fold greater than that of said parent Fc polypeptide.
14. (Original) An antibody according to claim 12, wherein said Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of 234, 235, 239, 240, 243, 264, 266, 328, 330, 332, and 325.

15. (Original) An antibody according to claim 14, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234E, 234Y, 234I, 235D, 235S, 235Y, 235I, 239D, 239E, 239N, 239Q, 239T, 240I, 240M, 243L, 264I, 264T, 264Y, 266I, 328M, 328I, 328Q, 328D, 328V, 328T, 330Y, 330L, 330I, 332D, 332E, 332N, 332Q, and 325T.
16. (Original) An antibody according to claim 15, wherein said Fc variant is selected from the group consisting of 264I, 243L/264I, 328M, 332E, 328M/332E, 264I/332E, 298A/332E, 239E/332E, 239Q/332E, 239E, 330Y, 332D, 328I/332E, 328Q/332E, 264T, 240I, 266I, 239D, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239Q/332D, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234E, 234Y, 234I, 235D, 235S, 235Y, 235I, 239T, 240M, 264Y, 330I, 325T, 328D/332E, 328V/332E, 328T/332E, 328I/332E, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.
17. (Original) An antibody according to claim 15, wherein said Fc variant further comprises at least one substitution at a position selected from the group consisting of 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.
18. (Original) An antibody according to claim 1 or 2, wherein said parent Fc polypeptide is substantially human, substantially mouse, substantially rat, or substantially monkey.
19. (Original) An antibody according to claim 1 or 2, wherein binding to one or more Fc ligands is unaltered.
20. (Original) An antibody according to claim 19, wherein said Fc ligand is selected from the group consisting of C1q, FcRn, protein A, and protein G.
21. (Original) An antibody according to claim 1 or 2, wherein CDC is unaffected.
22. (Original) An antibody according to claim 1 or 2, wherein binding to one or more Fc ligands is altered.

23. (Original) An antibody according to claim 1, wherein said Fc variant has a Fc γ RIIIa-fold:Fc γ RIIb-fold ratio greater than 1.
24. (Original) An antibody according to claim 23, wherein said Fc variant has a Fc γ RIIIa-fold:Fc γ RIIb-fold ratio greater than approximately 11:1.
25. (Original) An antibody according to claim 24, wherein said Fc variant has a Fc γ RIIIa-fold:Fc γ RIIb-fold ratio between approximately 11:1 and approximately 86:1.
26. (Original) An antibody according to claim 23, wherein said Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 234, 235, 239, 240, 264, 296, 330, and I332.
27. (Original) An antibody according to claim 26, wherein said Fc variant comprises at least one substitution selected from the group consisting of: 234Y, 234I, 235I, 239D, 239E, 239N, 239Q, 240A, 240M, 264I, 264Y, 296Q, 330L, 330Y, 330I, 332D, and 332E.
28. (Original) An antibody according to claim 27, wherein said Fc variant is selected from the group consisting of 332E, 264I/332E, 239E/332E, 239Q/332E, 296Q, 330L, 330Y, 332D, 239D, 239D/332E, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234Y, 234I, 235I, 240A, 240M, 264Y, 330I, 239D/330L/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.
29. (Original) An antibody according to claim 26, wherein said Fc variant further comprises one or more substitutions at a position selected from the group consisting of 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.
30. (Original) An antibody according to claim 1, wherein said Fc variant binds to at least one Fc γ R with reduced affinity relative to the parent Fc polypeptide.
31. (Original) An antibody according to claim 30, wherein said Fc γ R is Fc γ RIIIa.
32. (Original) An antibody according to claim 31, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239E, 239N, 239Q, 239F, 239H, 239Y, 240A, 240T, 241W, 241L, 241Y, 241E, 241R, 243W, 243L, 243Y, 243R, 243Q, 244H, 245A, 247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L,

- 264I, 264W, 264T, 264R, 264F, 264M, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H, 265T, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325V, 325H, 327N, 327L, 328M, 328E, 328N, 328Q, 328F, 328H, 328A, 329F, 330L, 330V, 330F, 330R, 330H, 332N, 332Q, 332T, 332H, 332Y, and 332A
33. (Original) An antibody according to claim 31, wherein said Fc variant is selected from the group consisting of 264L, 241W, 241L, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, 241L/262I, 243L/262I/264W, 241Y/243Y/262T/264T, 241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, 244H, 245A, 247V, 313F, 244H/245A/247V, 247G, 241E/243R/262E/264R/332E, 241E/243Y/262T/264R/332E, 265G, 265N, 239E/265G, 239E/265N, 239E/265Q, 296E, 296Q, 299I, 327N, 267Q/327S, 267L/327S, 327L, 329F, 330L, 297S, 297D, 297S/332E, 332N, 332Q, 264F, 263I, 299A, 299S, 299V, 325Q, 325L, 325I, 239N, 239F, 239N/332N, 239N/332Q, 239Q/332N, 239Q/332Q, 296D, 296N, 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239H, 239Y, 240A, 263T, 263M, 264M, 266A, 266T, 266M, 269H, 269Y, 269F, 269R, 296S, 296T, 296L, 296I, 298H, 299H, 330V, 330F, 330R, 330H, 325D, 325E, 325A, 325V, 325H, 328E/332E, 328N/332E, 328Q/332E, 328H/332E, 328A, 332T, 332H, 332Y, and 332A.
34. (Original) An antibody comprising a variant of a parent Fc polypeptide comprising at least one amino acid modification in the Fc region of said parent Fc polypeptide, wherein said Fc variant modulates effector function as compared to the parent Fc polypeptide.
35. (Original) An antibody according to claim 34, wherein said effector function is ADCC.
36. (Original) An antibody according to claim 35, wherein said Fc variant improves ADCC as compared to said parent Fc polypeptide.
37. (Original) An antibody according to claim 36, wherein said ADCC improvement is approximately 5-fold greater than that of said parent Fc polypeptide.

38. (Original) An antibody according to claim 37, wherein said ADCC improvement is between approximately 5-fold and 50-fold greater than that of said parent Fc polypeptide.
39. (Original) An antibody according to claim 37, wherein said Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 234, 235, 239, 240, 243, 264, 266, 328, 330, 332, and 325.
40. (Original) An antibody according to claim 39, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234E, 234Y, 234I, 235D, 235S, 235Y, 235I, 239D, 239E, 239N, 239Q, 239T, 240I, 240M, 243L, 264I, 264T, 264Y, 266I, 328M, 328I, 328Q, 328D, 328V, 328T, 330Y, 330L, 330I, 332D, 332E, 332N, 332Q, and 325T.
41. (Original) An antibody according to claim 39, wherein said Fc variant is selected from the group consisting of 264I, 243L/264I, 328M, 332E, 328M/332E, 264I/332E, 298A/332E, 239E/332E, 239Q/332E, 239E, 330Y, 332D, 328I/332E, 328Q/332E, 264T, 240I, 266I, 239D, 239D/332D, 239D/332E, 239D/332N, 239D/332Q, 239E/332D, 239E/332N, 239E/332Q, 239N/332D, 239N/332E, 239Q/332D, 330Y/332E, 264I/330Y/332E, 330L/332E, 264I/330L/332E, 234E, 234Y, 234I, 235D, 235S, 235Y, 235I, 239T, 240M, 264Y, 330I, 325T, 328D/332E, 328V/332E, 328T/332E, 328I/332E, 239E/264I/332E, 239Q/264I/332E, 239E/264I/330Y/332E, 239D/330Y/332E, 239N/330Y/332E, 239D/330L/332E, 239N/330L/332E, 264I/298A/332E, 239D/298A/332E, 239N/298A/332E, 239D/264I/332E, 239D/264I/298A/332E, and 239D/264I/330L/332E.
42. (Original) An antibody according to claim 39, wherein said Fc variant further comprises at least one substitution at a position selected from the group consisting of 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.
43. (Original) An antibody according to claim 39, wherein said parent Fc polypeptide is substantially human, substantially mouse, substantially rat, or substantially monkey.
44. (Original) An antibody according to claim 35, wherein said Fc variant reduces ADCC as compared to said parent Fc polypeptide.

45. (Original) An antibody according to claim 44, wherein said Fc variant comprises at least one substitution selected from the group consisting of 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239E, 239N, 239Q, 239F, 239H, 239Y, 240A, 240T, 241W, 241L, 241Y, 241E, 241R, 243W, 243L, 243Y, 243R, 243Q, 244H, 245A, 247V, 247G, 262I, 262A, 262T, 262E, 263I, 263A, 263T, 263M, 264L, 264I, 264W, 264T, 264R, 264F, 264M, 264E, 265G, 265N, 265Q, 265Y, 265F, 265V, 265I, 265L, 265H, 265T, 266A, 266T, 266M, 267Q, 267L, 269H, 269Y, 269F, 269R, 296E, 296Q, 296D, 296N, 296S, 296T, 296L, 296I, 296H, 297S, 297D, 297E, 298H, 299I, 299L, 299A, 299S, 299V, 299H, 299F, 299E, 313F, 325Q, 325L, 325I, 325D, 325E, 325A, 325V, 325H, 327N, 327L, 328M, 328E, 328N, 328Q, 328F, 328H, 328A, 329F, 330L, 330V, 330F, 330R, 330H, 332N, 332Q, 332T, 332H, 332Y, and 332A.
46. (Original) An antibody according to claim 44, wherein said Fc variant is selected from the group consisting of 264L, 241W, 241L, 243W, 243L, 241L/243L/262I/264I, 241W/243W, 241W/243W/262A/264A, 241L/262I, 243L/262I/264W, 241Y/243Y/262T/264T, 241E/243R/262E/264R, 241E/243Q/262T/264E, 241R/243Q/262T/264R, 241E/243Y/262T/264R, 328M, 328E, 328F, 244H, 245A, 247V, 313F, 244H/245A/247V, 247G, 241E/243R/262E/264R/332E, 241E/243Y/262T/264R/332E, 265G, 265N, 239E/265G, 239E/265N, 239E/265Q, 296E, 296Q, 299I, 327N, 267Q/327S, 267L/327S, 327L, 329F, 330L, 297S, 297D, 297S/332E, 332N, 332Q, 264F, 263I, 299A, 299S, 299V, 325Q, 325L, 325I, 239N, 239F, 239N/332N, 239N/332Q, 239Q/332N, 239Q/332Q, 296D, 296N, 234D, 234N, 234Q, 234T, 234H, 234V, 234F, 235N, 235Q, 235T, 235H, 235V, 235F, 239H, 239Y, 240A, 263T, 263M, 264M, 266A, 266T, 266M, 269H, 269Y, 269F, 269R, 296S, 296T, 296L, 296I, 298H, 299H, 330V, 330F, 330R, 330H, 325D, 325E, 325A, 325V, 325H, 328E/332E, 328N/332E, 328Q/332E, 328H/332E, 328A, 332T, 332H, 332Y, and 332A.
47. (Original) An antibody comprising an aglycosylated Fc variant of a parent Fc polypeptide comprising at least one amino acid modification in the Fc region of said parent Fc polypeptide, wherein said aglycosylated Fc variant has improved stability, solubility, or binding affinity to an Fc ligand relative to the aglycosylated form of said parent Fc polypeptide.

48. (Original) An antibody according to claim 47, wherein said aglycosylated Fc variant has improved binding affinity to an Fc ligand as compared to the aglycosylated form of the parent Fc polypeptide.
49. (Original) An antibody according to claim 48, wherein said Fc ligand is an FcγR.
50. (Original) An antibody according to claim 49, wherein said FcγR is FcγRIIIa.
51. (Original) An antibody according to claim 48, wherein said improved binding affinity is within 0.4-fold of the glycosylated form of the parent Fc polypeptide.
52. (Original) An antibody according to claim 47, wherein said Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 239, 241, 243, 262, 264, 265, 296, 297, 330, and 332.
53. (Original) An antibody according to claim 52, wherein said Fc variant comprises one or more substitutions selected from the group consisting of 239D, 239E, 241Y, 243Y, 262T, 264T, 264E, 265Y, 265H, 296N, 297D, 330Y, and 332E.
54. (Original) An antibody according to claim 52, wherein said Fc variant is selected from the group consisting of 297D/332E, 241Y/243Y/262T/264T/297D/332E, 239D/297D/332E, 239E/297D/332E, 239D/265Y/297D/332E, 239D/265H/297D/332E, 264E/297D/332E, 296N/297D/332E, and 297D/330Y/332E.
55. (Original) An antibody according to claim 53, wherein said aglycosylated Fc variant portion comprises at least one substitution at a position corresponding to a position of the human sequence selected from the group consisting of: 256, 270, 290, 298, 312, 322, 326, 329, 331, 333, 334, and 339.
56. (Original) An antibody according to claim 1 comprising a Fc fusion comprising said Fc variant.
57. (Original) An antibody according to claim 1 or 56, wherein said antibody further comprises an engineered glycoform.
58. (Original) An antibody according to claim 57, wherein said engineered glycoform improves effector function.

59. (Original) A pharmaceutical composition comprising an antibody according to claim 1 and a pharmaceutically acceptable carrier.
60. (Original) A method of treating a mammal in need of said treatment, comprising administering an antibody of claim 1.
61. (Original) An antibody comprising an Fc variant, said Fc variant comprises at least one substitution selected from the group consisting of: 332D, 332E, 332N, or 332Q, wherein said positions corresponding to the human sequence position, wherein said antibody has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
62. (Original) An antibody comprising an Fc variant, said Fc variant comprises at least one substitution selected from the group consisting of 264I, 264T, or 264Y, wherein said positions corresponding to the human sequence position, wherein said antibody or Fc fusion has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
63. (Original) An antibody comprising an Fc variant, said Fc variant comprises at least one substitution selected from the group consisting of 239D, 239E, 239N, 239Q, or 239T, wherein said positions corresponding to the human sequence position, wherein said antibody or Fc fusion has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
64. (Original) An antibody comprising an Fc variant, said Fc variant comprises at least one substitution selected from the group consisting of 330Y, 330L, or 330I, wherein said positions corresponding to the human sequence position, wherein said antibody or Fc fusion has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.

65. (Original) An antibody comprising an Fc variant, said Fc variant comprises at least one substitution selected from the group consisting of 240I or 240M, wherein said positions corresponding to the human sequence position, wherein said antibody or Fc fusion has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
66. (Original) An antibody comprising an Fc variant, said Fc variant comprises a substitution consisting of 297D, wherein said position corresponds to the human sequence position, wherein said antibody or Fc fusion has specificity for a target antigen selected from the group consisting of CD20, CD22, CD33, CD52, Her2/neu, EGFR, EpCAM, MUC1, GD3, CEA, CA 125, HLA-DR, TNFalpha, and VEGF.
67. (Original) An antibody according to claims 61, 62, 63, 64, 65 or 66 wherein said Fc variant additionally comprises the substitutions 298A.
68. (New) An antibody variant of a parent antibody, said antibody variant comprising two or more amino acid modifications in the Fc region of said parent antibody, wherein said antibody variant has improved ADCC in the presence of human effector cells as compared to the parent antibody.
69. (New) An antibody variant of a parent antibody, said antibody variant comprising two or more amino acid modifications in the Fc region of said parent antibody, wherein said antibody variant has improved ADCC in the presence of human effector cells as compared to WT IgG1.
70. (New) The antibody or Fc fusion according to claim 69, wherein said Fc region is a human IgG Fc region.
71. (New) The antibody or Fc fusion of claim 70, wherein said Fc region is a human IgG1 Fc region.
72. (New) The antibody or Fc fusion of claim 70, wherein said Fc region is a human IgG2 Fc region.

73. (New) The antibody or Fc fusion of claim 70, wherein said Fc region is a human IgG3 Fc region.
74. (New) The antibody or Fc fusion of claim 70, wherein said Fc region is a human IgG4 Fc region.